REMARKS

Claims 1-22 are pending. Claims 16-19 are withdrawn from consideration. Claim 2 has been canceled. Claims 1 and 3-22 remain in the case.

Claims 16-19 currently remain withdrawn from consideration. They have not been canceled, however, as they are properly examined with product claims 1-15, once the latter have been found allowable.[1]

Applicant notes that claims 2, 4 and 5 still are objected to as dependent on a rejected base claim, but are otherwise allowable. In addition, claims 8-15 are subject only to a rejection under the first paragraph of §112, and thus are free of the prior art.

The rejection of claims 1 and 6 under §102(b) based on Verheul *et al.*, and the rejection of claim 3 under §103(a) based on Verheul *et al.* in view of Anderson *et al.* both have been withdrawn.

Claim 2 is objected to under 37 C.F.R. 1.75(c) as being of improper dependent form for failing to further limit claim 1. Claim 2 has been canceled.

Claims 8-15 are rejected under the first paragraph of §112 as lacking enablement. The Examiner finds that the specification enables a fusion protein comprising a bispecific antibody that has a first specificity for CD20

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[1] *In re Ochiai*, 37 USPQ2d 1127 (Fed. Cir. 1995); *In re Brouwer*, 37 USPQ2d 1663 (Fed. Cir. 1996); "Training Materials for Treatment of Product and Process Claims in Light of *In re Brouwer* and *In re Ochiai*" (Office of Patent Policy Dissemination, Patent Academy).

and a second specificity for a region of IL-15α. She contends, however, that the specification does not enable a fusion protein comprising a bispecific antibody that has a first specificity for a cell marker "specific to a malignant cell" and a second specificity for a region of Il-15α, because "there are no specific cell markers known that are specific to malignant cells." She urges that "unless Applicants can show differences in expression of cell markers specific to malignant cells, and selective killing of malignant cells without killing those cells (expressing specific markers), that are required for normal function of the immune system," the enablement rejection will be maintained.

The Examiner notes applicants' argument that there is a large and growing body of experience in the use of antibodies to antigens expressed on malignant cells, such as the LL2 anti-CD22 mAb, to treat cancer. She does not, however, provide specific arguments in response to applicants' statements that

> while it is true that antibodies such as LL2 also will bind to non-malignant cells, binding is much higher for malignant cells. This is so because the malignant cells express the cognate antigen much more highly than do non-malignant cells. By merely managing the dose, it often is possible to kill malignant cells without unduly damaging non-malignant cells. In cases where higher doses are necessary to kill the malignant cells, adjunct therapy with cytokines and/or autologous bone marrow or peripheral stem cell rescue can be used as part of an effective therapy. Accordingly, one of ordinary skill in the art is clearly able to practice the present invention.

Should the Examiner persist in this rejection, it is requested that she provide her reasons why the above factual statements have not been found persuasive. Reconsideration and withdrawal of the rejection of claims 8-15 under the first paragraph of §112 is respectfully requested.

Claims 1, 6 and 7 stand rejected under §102(b) based on Mallinckrodt Medical. Mallinckrodt Medical is directed to "a labelled CXC chemokine [utilized] to ***image*** a target site in an animal's body" and does not suggest conjugates with a ***therapeutic*** radionuclide. The Examiner argues, however, that "a labeled CXC chemokine with a radioactive agent as a label to be used as a diagnostic, ***can be therapeutic if too much of the radionuclide conjugated to said cytokine is used*** (emphasis added). However, the only radionuclides disclosed in Mallinckrodt Medical are I-125, Tc-99m, Ga-67 and In-111. All of these radionuclides are useless for therapy, *i.e.*, even were a large amount of radionuclide-labelled conjugate to be used, a therapeutic effect would not ensue. Moreover, Mallinckrodt Medical specifically teaches the use of "a diagnostically effective dosage" which will "vary depending on considerations such as age, condition, sex and extent of disease in the subject individual, counter indications, if any, and variables." The use of "too much" radionuclide, such that a therapeutic effect might occur, is not fairly taught. The Examiner's allegation that Mallinckrodt Medical anticipates the subject matter of claims 1, 6, and 7 is not well taken.

In view of the amendments to the claims and the foregoing remarks, it is believed that all claims are in

condition for allowance. Reconsideration of all rejections and a notice of allowance are respectfully requested. Should there be any questions regarding this application, Examiner Mertz is invited to contact the undersigned attorney at the phone number listed below.

Respectfully submitted,

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Date

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The Commissioner is hereby authorized to charge any fee required by the filing of this response to Deposit Account No. 19-0741.